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Advances in pharmacogenomics for personalized emergency medicine: Implications for drug safety and efficacy

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***Abstract*---Background:** Advances in pharmacogenomics are transforming personalized emergency medicine by addressing genetic variability in drug metabolism and response. Genetic variations can significantly affect drug safety and efficacy, particularly in emergency

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scenarios where rapid and effective treatment is critical. **Aim:** This review aims to explore how pharmacogenomics can enhance personalized emergency medicine, focusing on implications for drug safety and efficacy. **Methods:** We reviewed recent literature on pharmacogenomics, emphasizing its impact on drug responses in various clinical contexts including chronic diseases, autoimmune disorders, cancer, infectious diseases, psychiatric and neurologic conditions, and chronic pain. The review included case studies and clinical guidelines that integrate genetic testing into drug prescribing practices. **Results:** Pharmacogenomic research has identified numerous genetic variations influencing drug metabolism and efficacy. For instance, variations in genes such as CFTR, TPMT, BRCA1/2, and UGT1A1 can predict drug responses and adverse reactions, leading to more tailored and effective treatments. Implementation of pharmacogenomic testing has demonstrated potential in reducing adverse drug reactions and improving therapeutic outcomes across several conditions, including cystic fibrosis, cancer, and chronic pain. **Conclusion:** Incorporating pharmacogenomic data into emergency medicine practice offers significant benefits by personalizing treatment plans and minimizing adverse effects. Genetic testing can guide drug selection and dosing, enhancing both safety and efficacy. Ongoing research and integration of pharmacogenomic findings into clinical practice are essential for advancing personalized medicine.

***Keywords*---**pharmacogenomics, personalized medicine, drug safety, drug efficacy, genetic variations, emergency medicine.

Introduction

Numerous elements contribute to the onset of chronic diseases, including lifestyle habits, environmental exposures, social determinants, and, in some cases, genetic factors. Genetic mutations can heighten the likelihood of developing chronic conditions, with genetic predispositions being exacerbated by lifestyle choices or environmental and social influences. For instance, mutations in genes involved in lipid homeostasis such as LDLR, APOB, or PCSK9 can lead to familial hypercholesterolemia, thereby increasing the risk of early-onset cardiovascular diseases, although individuals may remain asymptomatic [1, 2]. The presence of these genetic mutations combined with tobacco use or obesity further amplifies the risk for cardiovascular conditions [3].

In the case of certain chronic disorders like cystic fibrosis, genetic polymorphisms alone can directly cause the disease. Cystic fibrosis is an autosomal recessive genetic disorder resulting from mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene [4]. Due to advancements in treatment and management, cystic fibrosis has evolved from a condition with high childhood mortality to a chronic illness with a life expectancy exceeding 40 years [4]. Other inherited genomic variations that can elevate the risk of chronic diseases include familial cardiomyopathy (e.g., mutations in heart muscle genes such as TNNI3,

TNNT2, MYH7), inherited neuropathies (e.g., mutations in myelin genes like PMP22, EGR2), Alzheimer's disease (e.g., mutations in genes associated with amyloid plaques such as APOE ε4), and cancer (e.g., mutations in genomic stability genes such as BRCA1, BRCA2, MSH6) [5,6,7,8].

Genetic polymorphisms not only contribute to the development of chronic diseases but also influence responses to pharmacological treatments. Patients with a single chronic condition are likely to be on at least one maintenance medication, while those with multiple chronic conditions may be prescribed ten or more drugs [9, 10]. Among individuals with the same chronic disease and similar medication regimens, responses to specific drugs or the occurrence of adverse drug reactions can vary significantly. Such variability in pharmacotherapy responses has been linked to genetic variations affecting drug metabolism (i.e., pharmacokinetics) or drug targets (i.e., pharmacodynamics) [11,12,13]. For instance, the CFTR gene, which encodes a chloride channel critical for ion and fluid transport, illustrates how genetic variations impact drug efficacy [4]. Over 1900 CFTR mutations have been identified, potentially disrupting CFTR protein biosynthesis, folding, trafficking, or causing the ion gate to remain predominantly closed [14]. Ivacaftor is a medication that promotes the opening of the ion gate, thereby benefiting only those cystic fibrosis patients with mutations like CFTR G551D that affect ion channel gating [14]. Depending on the drug and associated genetic variation, approximately 20–95% of the variability in drug responses can be attributed to genetic factors [11, 12].

Adverse drug reactions and inadequate responses to pharmacotherapy are significant contributors to morbidity and mortality. Serious or fatal adverse drug reactions impact millions of patients annually and are considered a leading cause of death in the US [15, 16]. Patients with chronic conditions requiring multiple medications face a higher risk of adverse drug events. Identifying genetic variations associated with drug effectiveness and potential adverse drug reactions could significantly reduce morbidity and mortality linked to gene-drug interactions [17].

Pharmacogenetics, which examines how genetic variations affect drug responses, was first identified in the 1950s concerning observed differences in drug metabolism among individuals [18,19,20]. Single nucleotide polymorphisms (SNPs) are the most commonly identified genetic variations influencing drug response. SNPs may lead to loss of protein function or, if located in regulatory regions, alter gene expression [21,22,23]. The initial sequencing of the human genome revealed over 40 million SNPs, with an estimated occurrence of one SNP per 600 DNA base pairs [24, 25]. Other genetic variations impacting drug response include DNA base pair insertions or deletions (indels), short DNA sequence repeats, and copy number variations (i.e., gene gain or loss) [26, 27]. The term allele refers to SNPs or other genetic variations present within a gene. Based on how these variations affect protein function, a phenotype may be classified as ultra-rapid, rapid, normal, intermediate, or poor metabolizer [28]. Generally, extreme phenotypes in the drug metabolic continuum have the most significant impact on pharmacotherapy outcomes.

For many chronic conditions, a variety of pharmacotherapies are available. For instance, major depressive disorder can be treated with tricyclic antidepressants, selective serotonin reuptake inhibitors, and serotonin-norepinephrine reuptake inhibitors. Even with adherence to guidelines and best practices, there are multiple therapeutic options [29, 30]. Each medication presents a unique side effect profile, and depending on an individual's genetic makeup, the risk of adverse effects can vary among drugs. By incorporating pharmacogenetic data similarly to kidney or liver function tests, rational drug prescribing strategies can be developed to select drugs with a lower risk of adverse events. For some gene-drug pairs, evidence linking genetic variations to drug responses is sufficiently robust to support clinical application [31,32,33].

Gene–Drug Considerations for Chronic Diseases

Extensive evidence establishes connections between genetic variations and chronic diseases, as well as the relationship between genetic polymorphisms and responses to pharmacotherapies. This section outlines several gene–drug pairs that are currently relevant in clinical practice or may be adopted in the near future.

Autoimmune Disorders

Several chronic autoimmune diseases, such as rheumatoid arthritis, lupus, and inflammatory bowel diseases, can be managed pharmacologically with thiopurine drugs. Azathioprine and mercaptopurine, both cost-effective medications, are commonly prescribed prior to the initiation of tumor necrosis factor-α inhibitors. Thiopurine methyltransferase (TPMT) metabolizes azathioprine and mercaptopurine into less active compounds [34, 35]. In the absence of TPMT activity, thiopurines are metabolized more rapidly to thioguanine nucleotides, which at elevated levels can induce bone marrow toxicity. Individuals with one non-functional TPMT allele (intermediate metabolizers) face a higher risk of myelosuppression, while those with two non-functional TPMT alleles (poor metabolizers) are at a significantly increased risk of severe myelosuppression if administered standard doses of thiopurines due to high thioguanine nucleotide levels. For intermediate metabolizers, a reduction in the initial dose of azathioprine or mercaptopurine by 30–60% is advised, with subsequent dose adjustments based on patient response [36, 37]. For poor metabolizers, it is recommended to cut the azathioprine or mercaptopurine dose by 90% and administer it three times per week instead of daily [36, 37].

Cancer

Cancer susceptibility and response to treatment can be influenced by both germline variations and somatic mutations. Germline polymorphisms, inherited from both parents, can increase cancer risk, while somatic mutations, acquired post-conception, contribute to tumor development. Variations in BRCA1 or BRCA2 genes elevate the risk for certain cancers but also increase responsiveness to poly(ADP-ribose) polymerase inhibitors such as olaparib [38,39,40]. Similarly, MSH6 polymorphisms raise the risk of Lynch syndrome (hereditary nonpolyposis colorectal cancer), where immunotherapy may be a viable treatment option [41].

In the context of hematologic malignancies like acute lymphocytic leukemia, mercaptopurine is used, and dosing strategies for TPMT intermediate and poor metabolizers are similar to those applied for autoimmune disorders [36, 37]. Dihydropyrimidine dehydrogenase, encoded by the DPYD gene, is responsible for the metabolism of the chemotherapeutic agent 5-fluorouracil [42]. Individuals with two non-functional DPYD alleles who are exposed to 5-fluorouracil may experience severe or even fatal toxicities [43, 44]. It is recommended that DPYD poor metabolizers avoid 5-fluorouracil, while a 50% dose reduction should be considered for intermediate metabolizers [43,44,45].

The analysis of tumor biopsies for somatic mutations is becoming increasingly routine, with somatic testing now standard practice for certain cancers (e.g., advanced lung cancer). For example, epidermal growth factor receptor (EGFR) mutations guide the use of EGFR-tyrosine kinase inhibitors (TKIs) in lung cancer treatment [46, 47]. EGFR exon 19 deletions can be targeted by EGFR-TKIs such as erlotinib, while EGFR T790M mutations are resistant to first- and second-generation TKIs but responsive to the third-generation EGFR-TKI osimertinib. The FLAURA trial demonstrated that osimertinib offers superior efficacy for specific EGFR mutations (e.g., EGFR L858R and EGFR exon 19 deletions) and is now recommended as frontline therapy for metastatic lung cancer with these mutations [48]. Precision oncology is transforming cancer treatment, as many targeted therapies are orally administered, present fewer severe side effects compared to older chemotherapeutic agents and may be more effective. The market is seeing an influx of targeted anti-cancer agents with specific mutation indications listed in their labels. As clinical trials increasingly focus on patients with specific somatic mutations regardless of tumor histology, the number of approved anti-cancer agents targeting particular somatic mutations is expected to expand [49].

Infectious Diseases

Although there is no cure for human immunodeficiency virus (HIV), antiretroviral therapy has significantly improved survival rates, with studies indicating that life expectancy for HIV-infected individuals may now be comparable to that of the general population [50,51,52]. Early initiation of antiretroviral therapy and adherence to medication are crucial for viral suppression and improved health outcomes. However, antiviral agents can cause severe and sometimes life-threatening side effects that may disrupt therapy or affect compliance.

Abacavir and Hypersensitivity Reactions

Abacavir, a nucleoside-analogue reverse-transcriptase inhibitor with strong antiviral activity, is frequently included in combination therapies for HIV. About 6% of individuals exposed to abacavir will experience a hypersensitivity reaction, which can be fatal in rare cases [53, 54]. Human leukocyte antigen B (HLA-B) plays a role in immune responses, including drug-induced hypersensitivity. Although the exact mechanism is not fully understood, it is believed that HLAs recognize drugs as foreign and present drug–peptide complexes to the immune system, triggering hypersensitivity reactions [55]. The HLA-B*57:01 allele is predictive of abacavir-induced hypersensitivity [56,57,58]. A study showed that*

*preemptive screening for HLA-B*57:01 significantly reduced the incidence of hypersensitivity reactions (3.4% in the genotyping group vs. 7.8% in the control group, p<0.001) [59]. The FDA now advises screening for HLA-B*57:01 before prescribing abacavir.

Atazanavir and Hyperbilirubinemia

Atazanavir, a protease inhibitor used in conjunction with other antiretrovirals for HIV treatment, can cause hyperbilirubinemia by inhibiting uridine diphosphate glucuronosyltransferase (UGT) 1A1, an enzyme responsible for bilirubin metabolism [60, 61]. Variants in the UGT1A1 promoter region, such as UGT1A1*28, reduce enzyme expression, leading to Gilbert's syndrome [23, 62]. Carriers of UGT1A1*28 who use atazanavir are more likely to experience treatment discontinuation due to hyperbilirubinemia, which can cause skin and eye discoloration [63, 64]. Incorporating preemptive genotyping for HLA-B*57:01 and UGT1A1 into HIV treatment algorithms could help identify individuals at risk for hypersensitivity reactions or treatment discontinuation, thereby refining drug prescribing strategies [54, 59, 65, 66].

Chronic Hepatitis C and Genotype-Based Therapy

Chronic hepatitis C infection, a leading cause of liver disease such as cirrhosis and hepatocellular carcinoma, is commonly treated with pegylated interferon-α and ribavirin. This regimen is associated with sustained virological response (SVR)—the absence of viremia 24 weeks post-treatment—which improves morbidity and mortality [67, 68]. However, 30–45% of patients fail to achieve SVR with this treatment [69,70,71,72]. Given the prolonged duration of therapy (up to 48 weeks) and its potential severe side effects, identifying patients likely to respond poorly is crucial. A genome-wide association study identified a SNP in IFNL3 (also known as IL28B) that predicts response to interferon-α therapy [72]. Patients with an unfavorable genotype have about a 30% chance of achieving SVR, whereas adding a protease inhibitor to the regimen can increase this likelihood to 60% [73]. Those with a favorable genotype may be eligible for a shortened treatment duration (24–28 weeks) [73]. While IFNL3 genotyping is currently used in clinical practice, newer antiviral regimens like ledipasvir/sofosbuvir are reducing the reliance on IFNL3 for hepatitis C treatment decisions.

Voriconazole and Genetic Variants

Invasive fungal infections, often observed in chronic conditions affecting immune defenses such as HIV and cystic fibrosis, are managed with antifungal agents like voriconazole. Voriconazole, the first-line treatment for aspergillosis, has a narrow therapeutic range (1–6 mcg/mL), with sub-therapeutic levels linked to progressive infections and poor outcomes [76, 77]. The enzyme CYP2C19 metabolizes voriconazole, and a SNP (c.-806C>T), known as CYP2C19*17, causes increased enzyme activity and higher metabolic capacity [22, 78]. Individuals with CYP2C19*17 may metabolize voriconazole more rapidly, leading to lower drug concentrations and an increased risk of progressive infections [76, 79, 80]. Genotyping CYP2C19 in at-risk populations could help identify those needing

higher initial doses of voriconazole or alternative antifungal treatments not metabolized by CYP2C19 [81, 82].

Psychiatric and Neurologic Conditions

Major Depressive Disorder and Pharmacogenomics

Major depressive disorder (MDD) is a leading cause of disease burden and may become the most prevalent condition in developed countries [83, 84]. It can be a chronic disorder or a comorbidity with other chronic diseases like cancer, chronic obstructive pulmonary disease, or congestive heart failure [85]. Initial therapy failure occurs in 30–50% of patients due to intolerance or ineffectiveness, and antidepressant-induced adverse events lead to over 25,000 emergency department visits annually in the US [86,87,88]. Many antidepressants are metabolized by polymorphic cytochrome P450 enzymes, such as CYP2D6 and CYP2C19. Evidence links CYP2D6 and CYP2C19 polymorphisms to pharmacokinetic parameters and treatment outcomes for selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs) [89,90,91]. Early clinical studies indicated that pharmacogenomic testing to guide antidepressant prescribing resulted in better response rates and cost-effectiveness compared to non-genotyped patients, though further research is needed [92,93,94,95]. Given high initial therapy failure rates and the lack of a universally effective drug, pharmacogenomic testing could become a standard practice in depression management [96, 97].

CYP2D6 and CYP2C19 Gene-Based Dosing Guidelines

For SSRIs and TCAs, dosing guidelines based on CYP2D6 and CYP2C19 genotypes are available [89,90,91]. CYP2D6 ultra-rapid metabolizers may experience therapeutic failure due to low drug plasma concentrations, necessitating the use of an SSRI or TCA not metabolized by CYP2D6. Conversely, CYP2D6 poor metabolizers are at higher risk of adverse drug effects from elevated plasma concentrations, and an initial 50% dose reduction is recommended with gradual titration based on response. Similar guidelines apply to CYP2C19 ultra-rapid or poor metabolizers for SSRIs and TCAs metabolized by CYP2C19 [89, 90]. Although there are limited gene-based guidelines for other antidepressants metabolized by these enzymes, further guidelines are expected [98]. Additionally, research is emerging on the influence of serotonin receptor and transporter polymorphisms on antidepressant response [99, 100].

Pharmacogenomics in Neurologic Disorders

Clobazam

Clobazam, used for Lennox-Gastaut syndrome, requires lifelong management of seizures. CYP2C19 poor metabolizers are exposed 3–5 times more to n-desmethylclobazam, potentially increasing the risk of side effects [101]. The FDA recommends a 50% initial dose reduction for CYP2C19 poor metabolizers, with careful titration based on clinical response.

Cholinesterase Inhibitors

Cholinesterase inhibitors, such as donepezil and galantamine, are used to treat Alzheimer's disease. Both drugs are metabolized by CYP2D6, but current evidence does not strongly correlate CYP2D6 genotype with drug response [102]. CYP2D6 poor metabolizers may experience greater exposure to galantamine, necessitating cautious dose titration.

Tetrabenazine

Tetrabenazine, used for treating chorea associated with Huntington's disease, may induce side effects like suicidality in CYP2D6 poor metabolizers, especially at higher doses [103]. The drug insert advises CYP2D6 genotyping before dose escalation, recommending a maximum single dose of 25 mg and a daily limit of 50 mg for poor metabolizers.

Carbamazepine

Carbamazepine is used for various chronic conditions including seizures and neuropathic pain. It can cause severe side effects such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), which can be fatal in up to 30% of cases. A study found that all patients with SJS were positive for the HLA-B*15:02 allele [104]. Subsequent research confirmed that HLA-B*15:02 carriers are approximately 100-fold more likely to develop SJS/TEN, though the positive predictive value is around 8% [105]. A prospective study of 4,335 individuals demonstrated that preemptive HLA-B*15:02 genotyping completely prevented SJS/TEN by guiding the use of alternative medications [106]. The FDA now recommends HLA-B*15:02 screening before prescribing carbamazepine.

Chronic Pain

Chronic pain affects approximately one in three individuals in the US [107]. Genetic variations in genes involved in pain perception, drug metabolism, transport, and targets can influence treatment response [108]. For instance, about two-thirds of the variability in morphine response can be attributed to genetic differences [109]. Catechol-O-methyltransferase (COMT) regulates dopamine, epinephrine, and norepinephrine in the pain perception pathway [110]. Four single nucleotide polymorphisms (SNPs) in COMT may affect pain sensitivity, predicting low, average, or high sensitivity based on the number of SNPs present [111,112,113]. However, clinical data supporting the use of COMT genotypes for opioid therapy guidance remain limited [114].

Treatment for chronic pain varies based on its type (e.g., neuropathic vs. nociceptive pain) and severity. Tricyclic antidepressants, often used at low doses, can be effective for neuropathic pain. CYP2D6 ultra-rapid metabolizers might experience reduced efficacy of drugs like amitriptyline due to rapid metabolism leading to low drug plasma concentrations [90, 91]. Conversely, CYP2D6 poor metabolizers may not require dose adjustments as lower doses typically do not pose a risk of high drug concentrations. For higher doses of tricyclics, gene-based dosing strategies may be helpful.

Nonsteroidal anti-inflammatory drugs (NSAIDs), such as celecoxib, are used for chronic pain conditions like arthritis. Celecoxib is metabolized by CYP2C9, and variants such as CYP2C*2 and CYP2C9*3, which reduce enzyme function, are associated with prolonged drug elimination [115]. The FDA recommends a 50% dose reduction for known CYP2C9 poor metabolizers, and guidelines from the Clinical Pharmacogenetics Implementation Consortium suggest adjusting NSAID therapy based on CYP2C9 genotype [116].

Opioids are commonly prescribed for chronic pain. Codeine, a prodrug converted to morphine by CYP2D6, has been associated with fatal overdoses in children who are CYP2D6 ultra-rapid metabolizers [117]. Other opioids metabolized by CYP2D6 include tramadol, hydrocodone, and oxycodone. For CYP2D6 ultra-rapid metabolizers, non-CYP2D6-metabolized pain medications should be considered. Conversely, CYP2D6 poor metabolizers may find reduced efficacy with opioids like tramadol, codeine, hydrocodone, and oxycodone [114, 118]. Polymorphisms in the μ-opioid receptor (OPRM1), such as OPRM1 A118G, are linked to higher opioid dose requirements [119, 120], though clinical data on using OPRM1 genotypes to guide opioid dosing are still limited [114].

Cardiovascular Disease

Cardiovascular disease, a leading cause of morbidity and mortality, accounts for roughly one in three deaths in the US [121]. Hypertension is a significant risk factor, with genetic polymorphisms influencing responses to antihypertensive medications. Patients with Northern European ancestry generally respond better to angiotensin-converting enzyme inhibitors and β-blockers, while those with West African ancestry respond more favorably to calcium-channel blockers and diuretics, likely due to genetic differences affecting plasma renin activity [122,123,124]. Variants in NEDD4L are associated with sodium retention and hypertension, leading to lower responses to thiazide diuretics [126,127,128]. Variants in ADRB1, such as rs1801252 and rs1801253, are linked to reduced β-blocker response [129,130,131]. Practical applications of hypertension pharmacogenomics are limited, possibly due to the low effect size of individual variants. Combining gene studies and polygenic risk scores may help create a more significant effect size for personalized antihypertension treatments.

Dyslipidemia is another modifiable cardiovascular risk factor. Familial hypercholesterolemia (FH), an inherited disorder, is characterized by high LDL cholesterol levels. Variants in LDLR account for 79% of FH cases, followed by ApoB, PCSK9, and LDLRAP1 variants [132]. Statins are commonly used to treat dyslipidemia, but patients with variants in HMGCR and LDLR experience smaller reductions in LDL levels compared to non-carriers [133]. The SLCO1B1 variant rs4149056 impairs the hepatic uptake of statins and reduces LDL-lowering effects, particularly with rosuvastatin, pravastatin, and simvastatin [134,135,136]. This variant is also associated with increased myopathies for simvastatin users [137]. Dosing guidelines are available for simvastatin and SLCO1B1 [138, 139].

Antiplatelet therapy with aspirin, clopidogrel, prasugrel, or ticagrelor is used to prevent ischemic events after acute coronary syndrome (ACS) and percutaneous

coronary intervention. Clopidogrel is activated by CYP2C19, and poor metabolizers face increased risks of therapeutic failure due to ineffective activation [140, 141]. A meta-analysis indicated that CYP2C19*2 variant carriers have a higher risk of major cardiovascular events and stent thrombosis compared to wild-type patients, with hazard ratios varying for heterozygotes and homozygotes. This effect is most pronounced in high-risk ACS patients. Dosing guidelines are available for clopidogrel and CYP2C19 [140, 141].

Warfarin, a standard treatment for atrial fibrillation, is metabolized mainly by CYP2C9, with variants *2 and *3 associated with lower dose requirements and increased bleeding risks, particularly in individuals of European ancestry [142, 143]. In African ancestry populations, other variants like CYP2C9*5, *8, and *11 are more common [144, 145]. VKORC1 variants affect warfarin dosing by altering vitamin K metabolism. The FDA provides dosing recommendations for warfarin based on CYP2C9 and VKORC1 genotypes, with guidelines from the Clinical Pharmacogenetics Implementation Consortium [145]. The EU-PACT and COAG trials evaluated genetically guided warfarin dosing but yielded conflicting results. The EU-PACT trial, predominantly white, reported better outcomes with genetic guidance, while the COAG trial, with a more diverse population, found no significant differences. Neither trial included genotyping for CYP2C9*5, *6, *8, or *11, which could improve dosing predictions, especially in African Americans [140].

Conclusion

The field of pharmacogenomics has made substantial strides in enhancing personalized emergency medicine by linking genetic variations with drug responses. This connection is crucial for improving both the safety and efficacy of pharmacological treatments in emergency settings. As outlined, genetic polymorphisms can dramatically influence individual responses to medications, affecting both therapeutic outcomes and the likelihood of adverse drug reactions. In chronic conditions such as cystic fibrosis and cancer, pharmacogenomic insights have led to more targeted therapies, demonstrating how genetic variations like those in the CFTR, BRCA1/2, and UGT1A1 genes can guide effective drug use and reduce adverse effects. For instance, the identification of specific mutations allows for the tailoring of treatments, such as adjusting doses or choosing alternative drugs to mitigate side effects. This approach not only optimizes treatment efficacy but also enhances patient safety. Furthermore, pharmacogenomic testing has shown its potential in managing autoimmune disorders and psychiatric conditions by providing guidelines for dosing and drug selection based on genetic profiles. For example, the identification of TPMT variants helps adjust thiopurine doses to avoid myelosuppression, while CYP2D6 and CYP2C19 genotyping guide antidepressant therapy to reduce adverse effects and improve response rates. In infectious diseases, such as HIV and chronic hepatitis C, pharmacogenomics facilitates the selection of appropriate antiviral therapies and minimizes severe side effects, improving patient outcomes. The integration of genetic testing for drugs like abacavir and 5-fluorouracil demonstrates how pharmacogenomics can refine treatment strategies and prevent potentially fatal reactions. Despite these advancements, challenges remain in integrating pharmacogenomic data into routine clinical practice. Barriers include

the need for broader adoption of genetic testing, the development of standardized guidelines, and the need for continuous research to expand our understanding of gene-drug interactions. Overall, the incorporation of pharmacogenomic data represents a significant advancement in personalized emergency medicine. By tailoring drug therapy to individual genetic profiles, we can enhance treatment outcomes, reduce adverse effects, and ultimately improve patient care. Future research and clinical implementation will further solidify pharmacogenomics as a cornerstone of personalized medicine in emergency settings.

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تقدمات في علم الوراثيات الدوائية للطب الطارئ المخصص: تداعيات على أمان وفعالية الأدوية

الملخص:

الخلفية: تُحَوِّل التقدمات في علم الوراثيات الدوائية الطب الطارئ المخصص من خلال معالجة التباين الجيني في استقلاب الأدوية واستجابتها. يمكن أن تؤثر التغيرات الجينية بشكل كبير على أمان الأدوية وفعاليتها، خاصةً في السيناريوهات الطارئة حيث يكون العلاج السريع والفعال حاسمًا.

الهدف: يهدف هذا الاستعراض إلى استكشاف كيفية تحسين علم الوراثيات الدوائية للطب الطارئ المخصص، مع التركيز على التداعيات المتعلقة بأمان وفعالية الأدوية.

الطرق: قمنا بمراجعة الأدبيات الحديثة حول علم الوراثيات الدوائية، مع التركيز على تأثيره على استجابات الأدوية في سياقات سريرية مختلفة بما في ذلك الأمراض المزمنة، الاضطرابات المناعية الذاتية، السرطان، الأمراض المعدية، الحالات النفسية والعصبية، والألم المزمن. شمل الاستعراض دراسات حالة وإرشادات سريرية تدمج الاختبارات الجينية في ممارسات وصف الأدوية.

النتائج: حددت أبحاث علم الوراثيات الدوائية العديد من التغيرات الجينية التي تؤثر على استقلاب الأدوية وفعاليتها. على سبيل المثال، يمكن أن تتنبأ التغيرات في جينات مثلCFTR ، TPMT، BRCA1/2، و UGT1A1باستجابات الأدوية والتفاعلات الضارة، مما يؤدي إلى علاجات أكثر تخصيصًا وفعالية. أظهرت تنفيذ اختبارات علم الوراثيات الدوائية إمكانية تقليل التفاعلات الضارة للأدوية وتحسين النتائج العلاجية عبر حالات عدة، بما في ذلك التليف الكيسي، السرطان، والألم المزمن .

الخلاصة: يوفر دمج بيانات علم الوراثيات الدوائية في ممارسة الطب الطارئ فوائد كبيرة من خلال تخصيص خطط العلاج وتقليل الآثار الجانبية. يمكن أن توجه الاختبارات الجينية اختيار الأدوية وجرعاتها، مما يعزز الأمان والفعالية. البحث المستمر ودمج نتائج علم الوراثيات الدوائية في الممارسة السريرية أمران أساسيان لتقدم الطب المخصص.

الكلمات المفتاحية: علم الوراثيات الدوائية، الطب المخصص، أمان الأدوية، فعالية الأدوية، التغيرات الجينية، الطب الطارئ